1,023,393

PATENT SPECIFICATION

NO DRAWINGS

1,023,393

Date of Application and filing Complete Specification: April 17, 1964.
No. 16004/64.
Application made in Germany (No. F39566 IVa/30) on April 24, 1963.
Complete Specification Published: March 23, 1966.

Index at acceptance:—A5 E2; C3 C(1E1, 1E2); C3 P(7C7, 7C16B, 7C17, 7C18, 7D2A1, 10A, 10C7, 10C8B, 10C13A, 10C16B, 10C17, 10C18, 10C20D1, 10C20D3, 10D1A); C3 Q(A, C7, C16B, C17, C18B, F); C3 R(3C6, 3C8, 3C9, 3C10, 3C11, 3C17, 3D3, 3D10, 3D16, 29C6, 29C8, 29C10, 29C11, 29C12, 29C17, 32C10, 32C11, 32D2, 32G1, 32G2); D2 B13X

Int. Cl.:—A 61 l 13/00 // C 08 c, f, g, j, D 21 h

COMPLETE SPECIFICATION

Anti-Microbial Finishing of Materials

SPECIFICATION NO. 1,023,393

The inventors of this invention in the sense of being the actual devisers thereof within the meaning of Section 16 of the Patents Act, 1949 are: Hermann Genth, am Heckerhof 60, Krefeld, Germany, Fritz Steinfatt, Wiembachallee 5, Opladen, Germany, Otto Pauli, Friedrich-Ebertstrasse 321, Krefeld-Bockum, Germany, all of German nationality.

THE PATENT OFFICE

D 71194/5

at least the growth of microbes coming into contact with the material or even to kill these as completely as possible.

For the anti-microbial finishing of synthetic resins, there has already been suggested the addition of various substances, especially zinc pentachlorophenolate, possibly together with salicyl-anilide, or of tetramethyl-thiuram disulphide, chlorinated salicyl-anilides, trichlorophenol, organic mercury compounds or water-soluble mercury salts in admixture with phenols. However, these substances do not kill the microbes, in some cases even at comparatively high concentrations, but only inhibit their development and growth, whereas other agents, such as organic mercury compounds admittedly also kill some kinds of microbes but are of only limited applicability because of their high toxicity. Moreover, some of these substances, especially phenolic compounds, cause a still stronger killing action with a wider range, and does not cause discolorations of the materials by the action of light, is obtained when N-(dichlorofluoro-methyl-thio)-phthalimide is added to the materials.

If 1 per cent slurries of the two substances in propylene glycol are produced and small filter discs of the same size and type are saturated therewith, so that each disc contains the same amount of the slurry of the active substance, and if these discs are immediately placed on inoculated agar plates, then after a few days clear growth-inhibited zones result round the discs, and these zones can be measured in mm. as is generally customary in such tests.

After, for example, seven days' incubation of the plates, the following inhibited zones were measured in mm. in a comparison of the two substances:

1,023,393

PATENT SPECIFICATION

NO DRAWINGS

1,023,393

Date of Application and filing Complete Specification: April 17, 1964.
No. 16004/64.
Application made in Germany (No. F39566 IVa/30) on April 24, 1963.
Complete Specification Published: March 23, 1966.

Index at acceptance:—A5 E2; C3 C(1E1, 1E2); C3 P(7C7, 7C16B, 7C17, 7C18, 7D2A1, 10A, 10C7, 10C8B, 10C13A, 10C16B, 10C17, 10C18, 10C20D1, 10C20D3, 10D1A); C3 Q(A, C7, C16B, C17, C18B, F'); C3 R(3C6, 3C8, 3C9, 3C10, 3C11, 3C17, 3D3, 3D10, 3D16, 29C6, 29C8, 29C10, 29C11, 29C12, 29C17, 32C10, 32C11, 32D2, 32G1, 32G2); D2 B13X

Int. Cl.:—A 61 l 13/00 // C 08 c, f, g, j, D 21 h

COMPLETE SPECIFICATION

Anti-Microbial Finishing of Materials

We, FARBENFABRIKEN BAYER AKTIENGESELLSCHAFT, a body corporate organised under the laws of Germany, of Leverkusen-Bayerwerk, Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

It is known to bestow anti-microbial properties to the most varied materials, especially synthetic resins, by the addition of microbicidal substances. The anti-microbial finishing of material is intended to inhibit at least the growth of microbes coming into contact with the material or even to kill these as completely as possible.

For the anti-microbial finishing of synthetic resins, there has already been suggested the addition of various substances, especially zinc pentachlorophenolate, possibly together with salicyl-anilide, or of tetramethyl-thiuram disulphide, chlorinated salicyl-anilides, trichlorophenol, organic mercury compounds or water-soluble mercury salts in admixture with phenols. However, these substances do not kill the microbes, in some cases even at comparatively high concentrations, but only inhibit their development and growth, whereas other agents, such as organic mercury compounds admittedly also kill some kinds of microbes but are of only limited applicability because of their high toxicity. Moreover, some of these substances, especially phenolic compounds, cause disturbing discolorations of light-coloured, especially white, materials when exposed to the action of light.

Lastly it is known to employ N-(trichloromethyl thio-phthalimide for the anti-microbial finishing of materials of all kinds, for example leather, wood, fur goods, wool and textiles. This compound is not phytotoxic and is definitely suitable for the purpose mentioned.

We have now found that a likewise substantially non-toxic anti-microbial finishing of materials, which not only inhibits development and growth of germs, but also has a still stronger killing action with a wider range, and does not cause discolorations of the materials by the action of light, is obtained when N-(dichlorofluoro-methyl-thio)-phthalimide is added to the materials.

If 1 per cent slurries of the two substances in propylene glycol are produced and small filter discs of the same size and type are saturated therewith, so that each disc contains the same amount of the slurry of the active substance, and if these discs are immediately placed on inoculated agar plates, then after a few days clear growth-inhibited zones result round the discs, and these zones can be measured in mm. as is generally customary in such tests.

After, for example, seven days' incubation of the plates, the following inhibited zones were measured in mm. in a comparison of the two substances:

[*Price 4s. 6d.*]

	Asperg. niger	*Paecilomyces*	*Asperg. terreus*	*Penic. camerun.*	*Bct. coli*
Dichlorofluoro-compound	4	5	5	8	1
Trichloro-compound	1	3	2	4	0

	Bct. pyocyan.	*Stc. aureus*	*Stc. glycerin.*	*Bct. proteus*	*Candida albic.*
Dichlorofluoro-compound	0.5	4	3	2	8
Trichloro-compound	0	1	0	0	4

Not only the stronger effect of the fluorodichloro compound is recognised therefrom, but also a greater range of activity with bacteria. Admittedly it is already known from our Specification No. 927,834 to use N-(dichlorofluoro-methyl-thio) group containing compounds as plant protective agents, these compounds being distinguished from other known plant protective agents by an especially good fungicidal action. However, it was not to be foreseen that N-(dichlorofluoromethyl-thio)-phthalimide is also suitable for an anti-microbial finishing of materials for which it is important that the added microbicide, apart from the properties already mentioned, also possesses the broadest possible spectrum of activity so that it is not only active against fungi, as in plant protection, but also against yeast and bacteria. The anti-microbially finished materials according to the present invention are, in fact, not only outstandingly active against mould fungi and the wide-spread foot fungi, such *Trichophyton pedis* and *Candida albicans*, but also, and this is noteworthy, against many important bacteria, such as *Staphylicoccus aureus* and *Bacterium fluorescens*.

Materials which can be anti-microbially finished according to the present invention are, for example, the various synthetic resins, such as polyvinyl chloride, polystyrene, alkyd resins, polyester resins, natural and synthetic rubbers and polyurethanes, as well as cellulose and its conversion products, such as paper, cellulose acetate and cellulose acetobutyrate.

The amounts of N-(dichlorofluoro-methyl-thio)-phthalimide to be used can vary within wide limits and mainly depend upon the intended use of the material, upon its constitution and, to a small extent, also upon the temperature at which it is incorporated. In general, concentrations of 0.1 to 8 percent by weight, preferably 0.5 to 5 percent by weight, referred to the total weight of tion can be incorporated into the materials in the usual manner, for example, such as is usual for the incorporation of pigments, plasticisers and stabilisers. In all cases, care must be taken to ensure a uniform distribution in the material. When plasticisers are used, it is frequently advantageous to dissolve or disperse the active substance in the plasticiser and to incorporate these mixtures into the materials. In some cases, however, the active substance can also be added to the materials before the final moulding or possibly even during the production thereof.

The microbicidal action of the materials finished according to the present invention remains stable even to a frequently repeated prolonged treatment with the usual washing and cleaning agents. The stability of the action against leaching out can be tested by leaching synthetic resin test samples in water the material, suffice.

The N-(dichlorofluoro-methyl-thio)-phthalimide according to the present invenat 20°C. or at 45°C. and subsequent microbiological testing, for example according to the microbe carrier-contact process described in "Richtlinien für die Prüfung chemischer Desinfektionsmittel de Deutschen Gesellschaft für Hygiene und Mikrobiologie, Stuttgart, 1959, Page 8, paragraph 3, or page 10, paragraph 6."

Materials anti-microbially finished according to the present invention can be used for the production of objects for daily use of all kinds, especially those in which an effectiveness against bacteria and fungi of the most varied type, especially against foot and mould fungi, is important. They are especially suitable, for example, for the production of foils, floor coverings, handles, fittings, seatings and wall panellings, especially in public transport vehicles, physicians' waiting rooms and hospitals, and non-slip mats.

The following Examples are given for the purpose of illustrating the present invention,

the percentages being by weight. In the first four Examples the effectiveness of N-(dichlorofluoro-methyl-thio)-phthalimide is compared with the corresponding trichloro compound.

EXAMPLE 1

Two per cent of the active substances mentioned below are added to a polyurethane elastomer in the couse of the usual production process. The sheets prepared therefrom show the following inhibition zones on inoculated agar plates, measured in mm.:

	Asperg. terreus	*Chaetom. globosum*	*Stc. aureus*	*Bct. coli*	*Bct. proteus*	*Bac. mesent.*
Dichlorofluoro-compound	5	5	3	0.5	2	9
Trichloro-compound	2	0	2	0	0	3

EXAMPLE 2

Polyvinyl chloride, finished with 2 per cent of the two compounds in a comparable manner, gives the following areas of inhibition in mm.:

	Asperg. terreus	*Paecilomyces*	*Tricho. mentagre*	*Bct. coli*	*Bct. proteus*	*Stc. aureus*
Dichlorofluoro-compound	6	8	16	1	3	5
Trichloro-compound	1	5	12	0	2	4

EXAMPLE 3

The active substances specified in Examples 1 and 2 are added in various concentrations, calculated on the total solids content (binder + pigment), to a stoving lacquer of the following composition:

100 parts by weight castor oil alkyd resin (commercial resin: a reaction product of phthalic anhydride with glycerol and castor oil).

33 „ „ „ melamine resin (commercial resin: a reaction product of melamine and formaldehyde).

62 „ „ „ titanium dioxide (rutile)

1.2 „ „ „ calcium naphthenate

1 „ „ „ silicone oil

3 „ „ „ glycollic acid butyl ester

7 „ „ „ butanol.

With this lacquer, satinised cardboard is coated on both sides and, after stoving (20 minutes at 130°C), tested for resistance to mould by placing it on a nutrient salt agar and inoculating with a spore suspension of the following fungi:

Aspergillus niger
Pullularia pullulans
Alternaria species
Stachybotrys atara Corda
Aspergillus flavus
Aspergillus ustus
Paecilomyces varioti
Cladosporium herbarum
Penicillium citrinum

Evaluation takes place after 5 weeks' storage at 30°C.

The protective action against fungus is regarded as completely sufficient if the test

piece shows no trace of attack by fungus. It is designated as barely sufficient if the test piece shows no attack on its surface, but shows insignificant encroachment from the edge by the growth of the fungus from the nutrient medium. It is regarded as insufficient if the test piece shows growth on its surface, even if only in traces.

Addition, calculated on lacquer solids content	N-(Trichloromethyl-thio)-phthalimide	N-(Dichlorofluoro-methylthio)-phthalimide
0.5%	quite insufficient	barely sufficient
0.8%	not sufficient	„ „
1.3%	„ „	sufficient
2.0%	barely „	„

EXAMPLE 4

The two active substances are added in various concentrations to an air-drying alkyd resin lacquer of the following composition:

166 parts by weight of a commercial resin: a reaction product of phthalic anhydride with glycerol and fatty acids in form of a 60% benzene solution.

4 „ „ „ benzine
5.3 „ „ „ terpentinol

70 „ „ „ titanium dioxide (rutile)

3.7 „ „ „ calcium naphthenate

1 „ „ „ silicone oil

2.5 „ „ „ anti-skin forming agent

2.1 „ „ „ lead naphthenate (24% lead)

0.66 „ „ „ cobalt naphthenate (6% cobalt)

30 „ „ „ benzine-terpentinol 8:2.

The following results are obtained by carrying out tests as described above for resistance to mould on cardboard coated with the lacquer:

Addition, calculated on lacquer solids content	N-(Trichloromethyl-thio)-phthalimide	N-(Dichlorofluoro-methylthio)-phthalimide
0.75%	quite insufficient	not sufficient
1.0%	„ „	„ „
1.3%	„ „	barely „
1.7%	barely sufficient	sufficient

The next Examples show further possibilities of application of the present invention:

EXAMPLE 5

A dispersion of 1 part by weight N-(dichlorofluoro-methyl-thio)-phthalimide in 30 parts by weight of a polymeric plasti-

ciser based on adipic acid, 10 parts by weight phthalic acid dibutyl ester, 2 parts by weight titanium dioxide (rutile type) and 0.5 parts by weight chromium oxide green is stirred with 55.3 parts by weight powdered polyvinyl chloride. The mixture obtained is rolled to a foil at a temperature of 160-170°C.

In the microbe carrier-contact process, the so obtained foil proves to be effective against *Bacterium typhi, Bacterium paratyphi, Bacterium coli, Staphylicoccus aureus, Candida albicans, Trichophyton mentagrophytes, Aspergillus niger, Penicillium glaucum* and *Chaetomium globosum*.

The colour of the foil is not altered even after illumination for 300 hours with an ultraviolet lamp.

The microbicidal action of the synthetic resin finished in this manner is even stable against a regular, conventional treatment with washing and cleaning agents.

EXAMPLE 6

A dispersion of 2 parts by weight N-(dichlorofluoro-methyl-thio)-phthalimide in 35 parts by weight dioctyl phthalate is stirred with 2 parts by weight titanium dioxide (rutile type) and 60 parts by weight powdered polyvinyl chloride. The so obtained mixture is worked up to foils, profiles and sheets.

Even after a seven days' leaching at a bath ratio of 10:1 and a water temperature of 20°C., the water being changed every 24 hours, the articles have a killing action against *Bacterium coli* within a contact time of 16-20 hours. Even when leaching at 45°C. under otherwise identical conditions, a microbe-diminishing action against *Staphylococcus aureus* can still be clearly demonstrated within a contact time of 24-30 hours.

A foil produced as stated above is also unaltered in colour even after 300 hours' illumination with ultraviolet light.

EXAMPLE 7

For the anti-microbial finishing of a polyurethane foamed material the following procedure is used:

A foamed material is produced with toluylene diioscyanate from a polyester which may contain an accelerator and made from adipic acid, diethylene glycol and trimethylol propane, which has been mixed in two experiments with 1 and 2% N-(dichlorofluoro-methyl-thio)-phthalimide, respectively.

The anti-microbial action of the so obtained foamed materials can be demonstrated as follows by the formation of a zone of inhibition when test samples are placed upon inoculated agar nutrient substrata.

The finishings have a remarkable breadth of action:

	mm. inhibition zone after 5 days			
% active substance	*Paecilomyces*	*Aspergilus terreus*	*Trichophyton mentagrophytes*	*Candida albicans*
1	1	1	6	9
2	3	3	7	14
	Bacterium fluorescens	*Staphylococcus aureus*	*Bacterium coli*	*Bacillus mesentericus*
1	1	2	1	3
2	3	3	2	5

EXAMPLE 8

Into a usual formulation for foamed rubber mattresses based on natural latex, there are incorporated, before vulcanisation, 3 percent by weight N-(dichlorofluoro-methyl-thio)-phthalimide, referred to the weight of the rubber, and the vulcanisation is carried out in the usual manner.

The test samples placed upon inoculated nutrient agar plates show the following areas of inhibition in mm.:

Trichophyton mentagrophytes	*Candida albicans*	*Staphylococcus aureus*	*Bacterium fluorescens*	*Bacillus mesentericus*
9 (+)	5 (+)	3 (+)	16 (+)	6 (—)

+=microbe killing

—=no microbe killing

Most of the microbes are killed.

EXAMPLE 9

A conventional friction mixture for rubber boots based on crepe and soft, light-coloured rubber regenerate, is produced on the roller in the usual manner, with the addition of 1 percent by weight N-(dichlorofluoro-methyl-thio)-phthalimide and used for the frictioning. Vulcanisation is carried out by hot air heating for 90 minutes at 140°C.

When testing the anti-microbial values, the following results are obtained:

Microbe	inhibited area	microbe killing =+ no microbe killing =—
Trichophyton mentagrophytes	9	+
Candida albicans	5	+
Staphylococcus aureus	3	+
Bacterium fluorescens	16	+
Bacillus mesentericus	6	—

The pronounced microbial inhibition and microbial killing of this rubber finishing agains *Trichophyton mentagrophytes* and *Candida albicans*, which predominate in the case of fungal foot diseases proved to be especially valuable for the prevention of the infection and continuous reinfection by the microbes causing these diseases.

EXAMPLE 10

In the production of packing paper made from a wood pulp-cellulose mixture, so much N-(dichlorofluoro-methyl-thio) - phthalimide is added to the mass that the dry paper contains 2.0% of the active substance. The paper is thereby provided with a very good protection against mould fungi.

Test samples of this paper placed on nutrient agar dishes inoculated with mould fungi are not only not overgrown with mould fungi but form a broad zone of inhibition round themselves, as is shown by examples with the very growth-active and widespread mould fungi *Aspergillus terreus* and *Paecilomyces*.

Paper with 20% active substance	mm. inhibition zone after 12 days	
	Aspergillus terreus	Paecilomyces
	2 - 4	2 - 3

Paper test samples without the active substance are completely overgrown with the mould fungi after only 2 days.

WHAT WE CLAIM IS:—

1. Process for providing materials with an antimicrobial finish, wherein N-(dichlorofluoro-methyl-thio)-phthalimide is added to said materials.

2. Process according to claim 1, wherein 0.1 to 8% by weight of the thiophthalimide is used, referred to the total weight of the material.

3. Process according to claim 2, wherein 0.5 to 5% by weight of the thiophthalimide is used, referred to the total weight of the material.

4. Process according to claim 1 for providing materials with an anti-microbial finish, substantially as hereinbefore described and with reference to any of the specific Examples.

5. Materials, whenever provided with an anti-microbial finish by the process according to any of claims 1 to 4.

6. Anti-microbially finished materials, which are characterised by a content of N-(dichlorofluoro-methyl-thio)-phthalimide.

For the Applicants,
CARPMAELS & RANSFORD,
Chartered Patent Agents,
24 Southampton Buildings,
Chancery Lane, London, W.C.2.

Leamington Spa: Printed for Her Majesty's Stationery Office, by the Courier Press (Leamington) Ltd.—1966. Published by the Patent Office, 25 Southampton Buildings, London, W.C.2, from which copies may be obtained.